

## II. REMARKS

Claims 1-5 are pending. Claim 3 is withdrawn as being directed to non-elected subject matter. Claim 6 is canceled at this time.

Claim 6 is rejected under 35 U.S.C. § 112, second paragraph, for asserted indefiniteness and under 35 U.S.C. §§ 101 and 112, second paragraph, for improper definition of process. Applicants respectfully submit that these rejections are rendered moot by the above cancellation of claim 6. Accordingly, applicants respectfully request withdrawal of these rejections of claim 6.

Claims 1 (in part), 2, 4, and 5-6 (in part) are rejected under 35 U.S.C. § 103(a) as being obvious over Del Soldato et al. (WO 95/30641) in view of Ara et al. ("Cyclooxygenase and lipoxxygenase inhibitors in cancer therapy, " Prostaglandins, Leukotrienes and Essential Fatty Acids 54: 3-16 (1996)). This rejection is traversed.

Applicants submit that this rejection is rendered moot, in part, by the above cancellation of claim 6.

As to the remaining claims, applicants note that Del Soldato et al. discloses nitroderivatives of non-steroidal anti-inflammatory drugs (NSAIDs) having anti-inflammatory, analgesic and anti-thrombotic activities and agree with the Examiner that Del Soldato et al. "fail to disclose specifically treating gastrointestinal tumors" (Office Action, page 4, second to last full paragraph). However, Applicants submit that Ara et al. does not satisfy the deficiencies of Del Soldato et al.

Ara et al. merely discloses the use of NSAIDs, such as indomethacin, piroxicam and sulindac) in colon tumors and concludes that cyclooxygenase inhibition plays a

significant role in cancer growth, promotion and metastasis. As such, Ara et al. provides no teaching or motivation for those of skill in the art to indiscriminately alter the good action of the NSAIDs in cancer therapy, much less by linking a nitric acid ester to the NSAIDs and administering such nitroderivatives to treat colon tumors. As such, the presently claimed invention would not have been obvious to those of skill in the art in view of the cited references, alone or in combination.

Further, Applicants submit the previously filed Declaration under 35 U.S.C. § 1.132, which was filed on October 10, 2003, demonstrates the increased inhibition of precancerous cell formation in an experimental model of colon cancer by nitroderivative compounds of the presently claimed invention in comparison to the non-nitroderivative compound. A copy of the previously filed Declaration is enclosed for the Examiner's convenience. For example, as noted in Tables 1 and 2 increased inhibition of precancerous cell formation and decreased proliferation of cancer cells, respectively, are unexpectedly demonstrated by the elected species, 3-(nitroxymethyl)phenyl ester of aspirin, as compared to aspirin. Applicants respectfully submit that such evidence of unexpected results is sufficient to overcome the *prima facie* case of obviousness asserted in the Office Action.


Accordingly, for at least the above reasons, applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 (in part), 2, 4, and 5-6 (in part) under 35 U.S.C. § 103(a) as being obvious over Del Soldato et al. in view of Ara et al.

### III. CONCLUSION

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event this paper is not considered to be timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, referring to Attorney Docket No. 026220-00039. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300, referencing Attorney Docket No. 026220-00039.

Respectfully submitted,

  
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